15. (amended) The method of claim 11, wherein the [composition] peptidomimetic is a peptide of less than forty amino acids residues including amino acid residues 42 to 58 of [hu] human CD59.

18. (amended) The method of claim 10 wherein the [compound is a] peptidomimetic [compound comprising] comprises the side chains of [hu] human CD59 amino acid residues His^{44}, Asn^{48}, Asp^{49}, Thr^{51}, Thr^{52}, Arg^{55}, and Glu^{58} in [an equivalent spacial] the spatial orientation and alignment [to that presented on the surface] of hu CD59.

19. (amended) The method of claim 18 wherein the [spacial] spatial orientation and alignment of the side chains of His^{44}, Asn^{48}, Asp^{49}, Thr^{51}, Thr^{52}, Arg^{55}, and Glu^{58} in the compound are [equivalent to the spacial orientation and alignment] deduced by NMR structure determination.

Remarks

Amendments to the Specification

The specification has been amended to note trademarks. It is believed all sequences have already been identified by reference to sequence ID Numbers.

Response to Restriction Requirement

As noted above, review of the restriction requirement has been petitioned and all claims are still pending until the Petition is acted upon.

Rejection under 35 U.S.C. §112

Claims 10-12, and 16-17 were rejected on the basis that the claimed invention is not clearly enabled nor clearly defined in the application. These rejections are respectfully traversed.

The rejection appears to be based on the recitation "molecules structurally mimicking CD59 amino acids 42-58 when they are in a spatial orientation which inhibits formation of the hu C5b-9 complex when the compound is not hu CD59."

This language has been amended to refer to peptidomimetics having the structure and function of the region of CD59 amino acid residues 42-58 (page 11, lines 11-25). "Hu" has been replaced with human The claims should be interpreted in view of the extensive disclosure in the specification at pages 11 and 13-27, which describes molecules including proteins, antibodies, compounds identified using combinatorial, and compounds identified by rational drug design, using the guidelines provided based on the discovery that one short peptide sequence of human CD59 alone is responsible for the species-specific binding of CD59 to inhibit formation of the C5-b9 complex.

As the examiner is aware the standard for enablement and clarity is what one of skill in the art, would understand from the claims in view of the specification. Those skilled in the art would learn from the extensive examples that a very small region of human CD59 is responsible for CD59 species-specific role as a complement inhibitor. Indeed, the data at page 47 shows just how specific this role is, since substitution of amino acids to create the structure present in the analogous region of rabbit CD59 destroys the ability of the molecule to inhibit C5b-9 complex formation. The computer programs available at the time of filing provide extensive guidance once the data regarding the exact composition and spatial orientation and alignment provided by applicants has been entered into the program. Moreover, the assays can be used as a final determining factor – since the requirements for inhibition are so stringent, failure to inhibit formation of the human C5b-9 complex can be used as a rapid, simple screen.

Rejections under 35 U.S.C. §102 or 103

Claims 10-12 and 16-17 were rejected as disclosed by or obvious over U.S. Patent No. 5,550,108 to Sims, et al. Claims 10-12 and 16-17 were also rejected as obvious over the combination of Sims and Chang, et al., J. Biol. Chem.269(42), 26424-26430 (1994). These rejections are respectfully traversed.

Sims et al. is based on the discovery that CD59 inhibits complement activation, not just hemolysis, and notes that antibodies to C9 can be used to inhibit CD59 activity.

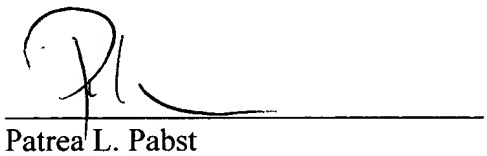
There is no disclosure of what region of CD59 imparts species-specificity. Merely because there may be an antibody which binds to C9 does not mean that it mimicks the region of CD59 which is in issue; in fact, absent making the antibody by immunization with this region, and then screening for efficacy in preventing human CD59 activity, it is extremely unlikely that such an antibody could be obtained. See in particular page 47 in this regard.

Chang is of no assistance in this regard. Chang identifies the region of human C9 which is bound by human CD59; not the portion of CD59 which binds. One cannot extrapolate from the information relating to human C9 to obtain information about human CD59. The identification of the critical amino acid sequence required careful analysis and many experiments.

In summary, none of the art discloses nor makes obvious the claimed compound which inhibits formation of the human C5b-9 complex, by imitating the structure and function of amino acid residues 42-58.

Allowance of all claims 10-19 is earnestly solicited. All claims 10-19 as currently pending are attached in an appendix to facilitate the examiner's review.

Respectfully submitted,



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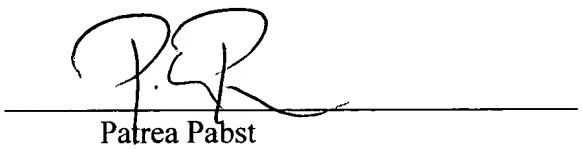
CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this , along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Date: November 8, 1999



Patrea Pabst

APPENDIX: PENDING CLAIMS 10-19 UPON ENTRY OF AMENDMENT

10. (amended) A method for inhibiting human C5b-9 complex assembly comprising ~~administering to a patient in need thereof~~ an effective amount of a composition [to increase CD59 inhibition of C5b-9 complex assembly wherein the composition includes] comprising a [compound selected from the group consisting of molecules structurally mimicking CD59 amino acid residues 42 to 58 which bind to C9 wherein the compound is not hu CD59] peptidomimetic having the structure and function of human CD59 amino acid residues 42-58.

11. (amended) The method of claim 10, wherein the [compound] peptidomimetic is selected from the group consisting of proteins, peptides, nucleic acids, and small molecules which bind specifically to amino acids 359 to 384 of [hu] human C9.

12. The method of claim 11, wherein the protein is an antibody.

13. (amended) The method of claim 11, wherein the protein is a chimeric peptide which [include] includes the amino acids 42 to 58 of the human sequence of CD59.

14. (amended) The method of claim 11, wherein the peptide is a covalently cyclized peptides comprising [hu] human CD59 amino acid residues 42 to 58.

15. (amended) The method of claim 11, wherein the [composition] peptidomimetic is a peptide of less than forty amino acids residues including amino acid residues 42 to 58 of [hu] human CD59.

16. The method of claim 10, wherein the composition further comprises a pharmaceutically acceptable carrier for administration to patients in need thereof.

17. The method of claim 10, wherein the patient is in need of suppression of complement-mediated inflammation.

18. (amended) The method of claim 10 wherein the [compound is a] peptidomimetic [compound comprising] comprises the side chains of [hu] human CD59 amino acid residues His^{44}, Asn^{48}, Asp^{49}, Thr^{51}, Thr^{52}, Arg^{55}, and Glu^{58} in [an equivalent spacial] the spatial orientation and alignment [to that presented on the surface] of hu CD59.

19. (amended) The method of claim 18 wherein the [spacial] spatial orientation and alignment of the side chains of His^{44}, Asn^{48}, Asp^{49}, Thr^{51}, Thr^{52}, Arg^{55}, and Glu^{58} in the compound are [equivalent to the spacial orientation and alignment] deduced by NMR structure determination.